AWARD NUMBER: W81XWH-16-1-0305

TITLE: Validation of Functional Reaching Volume as an Outcome Measure across the Spectrum of Abilities in Muscular Dystrophy

PRINCIPAL INVESTIGATOR: Linda Lowes, PhD

CONTRACTING ORGANIZATION: Research Institute at Nationwide Children's Hospital
Columbus, OH 43205

REPORT DATE: September 2017

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE		*Form Approved OMB No. 0704-0188*
1. REPORT DATE Sep 2017	**2. REPORT TYPE** Annual	**3. DATES COVERED** 1 Sep 2016 - 31 Aug 2017
4. TITLE AND SUBTITLE Validation of Functional Reaching Volume as an Outcome Measure across the Spectrum of Abilities in Muscular Dystrophy		**5a. CONTRACT NUMBER** **5b. GRANT NUMBER** W81XWH-16-1-0305 **5c. PROGRAM ELEMENT**
6. AUTHOR(S) Linda Lowes, PhD Lindsay Alfano, DPT, PCS E-Mail: Linda.Lowes@nationwidechildrens.org		**5d. PROJECT NUMBER** **5e. TASK NUMBER** **5f. WORK UNIT NUMBER**
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Research Institute at Nationwide Children's Hospital 700 Children's Dr Columbus, OH 43205-2664		**8. PERFORMING ORGANIZATION REPORT NUMBER**
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012		**10. SPONSOR/MONITOR'S ACRONYM(S)** **11. SPONSOR/MONITOR'S NUMBER(S)**
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited		
13. SUPPLEMENTARY NOTES		

14. ABSTRACT

ACTIVE measures functional reaching volume using the Microsoft Kinect camera while the participant plays an interactive video game regardless of ambulatory status. The objective of this project is to produce a trial ready outcome measure that will enable clinical trials to recruit subjects with a wider range of physical abilities and ages and address the limitation in current Duchenne muscular dystrophy outcomes. The specific aims were designed to improve the current ACTIVE system, determine the utility of integrating wireless motion sensors called Solitons into ACTIVE, and quantify the natural rate of change in FRV and determine the minimal clinically important difference (MCID). A comparison of ACTIVE and Solitons to the gold standard Vicon motion capture system showed the current ACTIVE system is more valid and reliable at the present time. Subject recruitment and data collection in ACTIVE is ongoing, including cross sectional and longitudinal data points in boys with DMD. Additionally, refinement of the Soliton software is underway to reassess the utility of Solitons in conjunction with ACTIVE.

15. SUBJECT TERMS					
16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF**	**18. NUMBER OF**	**19a. NAME OF RESPONSIBLE PERSON** USAMRMC
a. REPORT Unclassified	**b.ABSTRACT** Unclassified	**c. THIS PAGE** Unclassified	Unclassified	16	**19b. TELEPHONE NUMBER**

Standard Form 298 (Rev. 8-98)

TABLE OF CONTENTS

1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

Enrollment in clinical trials for individuals with Duchenne muscular dystrophy (DMD) is often dependent on the ability to walk independently since this is the primary efficacy outcome. These enrollment criteria exclude a large proportion of the population who no longer walk but may be willing to participate. Additionally, if a subject loses the ability to walk during a clinical trial, this subject's future data are lost. An outcome measure that measures a change in function on a continuous scale would improve access to clinical trials and minimize data loss. ACTIVE, a custom-designed video game using the Microsoft Kinect camera, measures functional reaching volume (FRV) across the spectrum of the disease in DMD regardless of ambulatory status. Our preliminary data support our hypothesis that FRV is a sensitive and functionally relevant outcome for DMD. In a study comparing participants with muscular dystrophy to a cohort of healthy control, ACTIVE was able to discriminately rank FRV across Brooke levels and from controls ($P < 0.001$). ACTIVE percent predicted volume was found to correlate highly with parental reports of daily activities ($r=0.454$; $P<0.05$) and mobility sections ($r=0.756$; $P<0.01$) of the Pediatric Evaluation of Disability Inventory (PEDI) indicating that FRV would be a meaningful outcome to the patient. Initial test-retest reliability of ACTIVE was also excellent (ICC=0.97; $P<0.0001$). In order to improve our current ACTIVE system and allow for implementation of ACTIVE across the lifespan in DMD in clinical trials, three areas were identified that could be further refined including 1) ensuring all individuals can be recorded, 2) improving the quantification of small movements, and 3) improving measurement accuracy. To this end, we collaborated with Dr. Furrukh Khan and Jessie Zhao, who developed miniature wireless motion capture sensors, known as Solitons to pair with the ACTIVE system. The following specific aims were developed to further enhance ACTIVE. The first is to expand the context of use of ACTIVE by utilizing the Soliton system. The second is to establish the natural rate of change and quantify the minimal clinically important difference (MCID) in FRV in males with DMD.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Outcome measure, Duchenne, wireless sensors, Kinect, video game, clinical trial readiness, neuromuscular disease, Soliton, functional reaching volume

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

Specific Aim 1	Timeline	Site 1	Consultant	Status
Major Task 1 **Expand the context of use of ACTIVE by utilizing the Soliton system.**	Months			
Local IRB Approval for Soliton use with ACTIVE: study protocol, recruitment plan	1-3	Dr. Lowes		Completed/ Approved 2/25/16
Local IRB Approval for verbal consent with information sheet with ACTIVE-Soliton functional reaching volume game	1-3	Dr. Lowes		Completed/ Approved 4/20/16
Development of 6 Soliton System	1-3		Dr. Kahn/ Ms. Zhao	Partially completed (30%)

Development of ACTIVE-Soliton functional reaching volume game	1-3	Research Information Services- Jeremy Patterson/ Steve Rust		Partially completed (80%)
Major Task 2 **Clinical testing and Refinement**				
Testing on 15 subjects with DMD and 15 healthy controls	4-6	Dr. Lowes	Dr. Kahn/ Ms. Zhao	Partially completed (10%)
Specific Aim 2				
Major Task 1 **Establish the natural rate of change in FRV in boys with DMD.**				
Collect longitudinal data with ACTIVE-Soliton	6-24	Dr. Lowes		Modified: Collect longitudinal data with ACTIVE Partially completed (30%)
Major Task 2 **Quantify the Minimal Clinically Important Difference (MCID) in FRV in boys with DMD.**				
Collect functional data and patient reported outcomes	6-24	Dr. Lowes		Partially completed (20%)

ACTIVE Quarterly Enrollment Tables

ACTIVE-Soliton System	**Year 1**				**Year 2**			
Target Enrollment of Subjects (per quarter)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
• Cross sectional subjects	---	15* control/ 15* DMD	25* DMD	25* DMD	25* DMD	25* DMD	10* DMD	---
	---	2 control†/ 5 DMD†	0†	0†				
• Longitudinal returning subjects 6 month follow up	---	---	---	12* DMD	23* DMD	23* DMD	23* DMD	---
				0†				
• Longitudinal returning subjects 12 month follow up	---	---	---	---	---	12* DMD	48* DMD	---
Cumulative Target Enrollment of Unique Subjects	**---**	**30***	**55***	**80***	**105***	**130***	**140***	**140***
		7†	0†	0†				

Projected quarterly enrollment* Actual quarterly enrollment†

ACTIVE System	**Year 1**	**Year 2**

Target Enrollment of Subjects (per quarter)	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
• Cross sectional subjects	---	15* control/ 15* DMD	25* DMD	25* DMD	25* DMD	25* DMD	10* DMD	---
	25 control/ 38 DMD	18 control/ 29 DMD†	23 control/ 17 DMD †	36 control/ 23 DMD †				
• Longitudinal returning subjects 6 month follow up	---	---	---	12* DMD	23* DMD	23* DMD	23* DMD	---
				33 DMD †				
• Longitudinal returning subjects 12 month follow up	---	---	---	---	---	12* DMD	48* DMD	---
Cumulative Target Enrollment of Unique Subjects	**---**	**30***	**55***	**80***	**105***	**130***	**140***	**140***
	63†	**110†**	**150†**	**209†**				

Projected quarterly enrollment* Actual quarterly enrollment†

What was accomplished under these goals?

Specific Aim 1 Accomplishments: Expand the context of use of ACTIVE by utilizing the Soliton system.

1) Gain approval from the local IRB to use Solitons in conjunction with ACTIVE.
   i. Gain local IRB approval for soliton use with ACTIVE
   The IRB at Nationwide Children's Hospital granted approval to allow the use of Solitons in conjunction with the ACTIVE system on 25 February 2016.

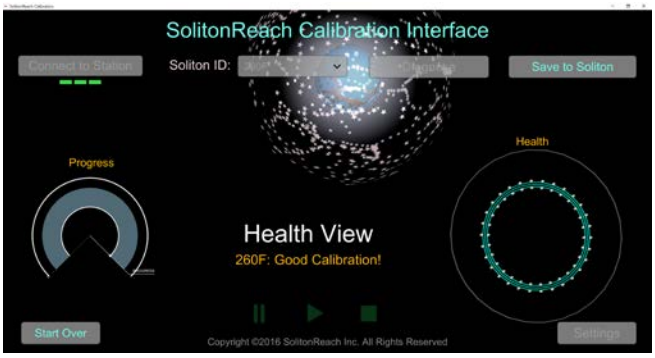
   ii. Gain local IRB approval for verbal consent after reviewing an information sheet with ACTIVE-Soliton functional reaching volume game
   The IRB at Nationwide Children's Hospital gave approval to use verbal consent to play the ACTIVE-Soliton functional reaching game after the subject and/or guardian has reviewed an information sheet detailing the study on 20 April 2016.

2) Integrate the Solitons into the ACTIVE system
   Develop Soliton System
   Dr. Kahn and Ms. Zhao delivered 6 Solitons to Dr. Lowes on 03 November 2016 for initial validation testing. After early testing several problems were discovered that would need to be corrected before they were useable in the clinic

   i. New Unity based Calibration Application
   A new calibration application was developed to improve the user experience. The new application also removes the dependence on MATLAB and instead uses Unity for enhanced graphics. Soliton sensors need to be calibrated before use. The calibration process requires users

to rotate a Solitons around in the environment it is going to be used. Since the original calibration app was designed for developers it was not friendly for non-technical users.

We improved the calibration application to be more user friendly based on the feedback from the clinical team.
The application now clearly shows if the calibration is successful or not through intuitive visual feedback. Calibration result can now be saved as a part of a comparison matrix during clinical trials. A screen shot of the application is shown below.



ii. Improved firmware for better Soliton-Station communication for Calibration

- During the calibration process the Soliton Station hardware writes calibration data back to a Soliton. Our original version of the Station firmware had a problem that occasionally this data would not be written back to a Soliton without the user being aware of it. This would lead the user to use un-calibrated Solitons under the false assumption that the Solitons were calibrated.
    - This problem has been fixed in the new version of the Station firmware, now the data is reliably written back to a Soliton each time it is calibrated.

iii. Improved handling of the Initial Pose Problem

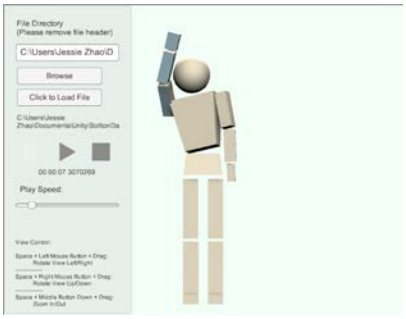
- To use the system accurately users are required to position themselves in a standard pose for system initialization. Originally the system was designed to have an initial pose with the patient keeping the back straight with both hands raise and pointing straight forward. Based on feedback from the clinical trial team we learnt that some patients with muscular dystrophy cannot put themselves into this standard pose.
    - A new initialization procedure was devised based on a 3D printed model. The system is now initialized with the Solitons placed on this model and not on the patient.
    - The new procedure works as follows:
        - Place the Solitons into keyed slots in the 3D printed model.
        - Initialize the system
        - Place the Soliton on patients. The patient need not assume a standard pose.
    - This initialization procedure helps in reducing the complexity in calibration

iv. Improved Repeatability

- During lab testing of Solitons, it was discovered that if a user seated on a revolving chair goes through a full rotation of the chair to return to the original position then a Soliton might not consistently give the same tracking result.
    - A new sensor algorithm was developed to address this problem

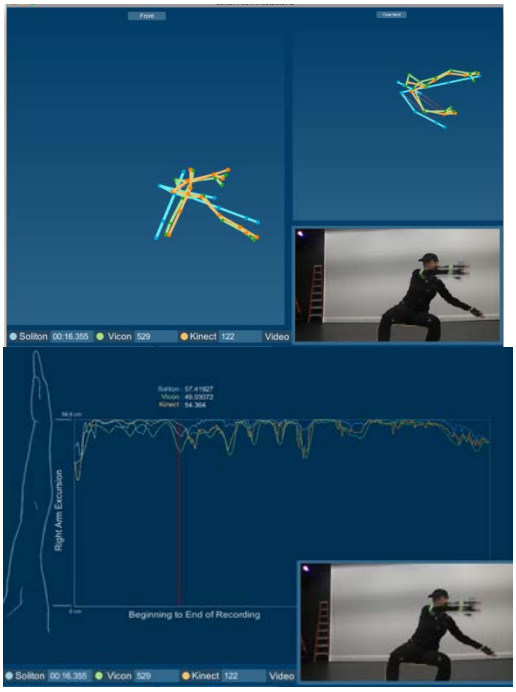
v. New Playback Software Tool

- A new data playback tool was developed to visually inspect the collected data. A screenshot of the tool is shown below.



Issues with individual Soliton sensor calibration, alpha-stage device firmware under active development and battery life identified a need for continued development and stabilization of the tooling and firmware of the Solitons before they could be used in the clinical or research setting. Batteries that are still light-weight but have a longer charge life replaced the previous type. John Luna collaborated with Dr. Kahn and Ms. Zhao to create a registration system that is more user-friendly. This development led to a device that would allow for all of the Solitons to be registered simultaneously rather than individually in future software versions. Although calibration is still performed one soliton at a time, this improvement improve increased the feasibility of using Solitons in a clinical or research setting and reduce the burden on the clinical evaluator. Due to the above encountered issues, the data from these trials was unable to be analyzed but did lead to the further refinement and improvement of the Solitons.

Comparison to the gold standard. The Solitons version 2 (v2) were compared to the current Kinect-based ACTIVE system and the gold-standard 12 camera Vicon motion capture system on 13 April 2017. A control subject performed reaching activities seated in an armless chair while the Soliton, ACTIVE, and Vicon systems simultaneously recorded data. Multiple trials were recorded and the subject was instructed to perform reaching motions in multiple directions, amplitudes, and speeds to mimic varying levels of function. Jeremy Patterson and his team developed an interface to convert the data from all three systems and interpose the three recordings over time to analyze the results. The Kinect system had a smaller measure of error compared to the Soliton system. The Soliton system frequently overestimated excursion compared to the Vicon system. In the figure on the right the Vicon recorded maximum right arm excursion as 49.03 cm compared to 54.36 cm and 57.42 cm by the Kinect and Soliton systems, respectively. Dr. Khan and Ms. Zhao are currently in the process of using the results of this analysis to improve the algorithms employed by Solitons to increase the accuracy.

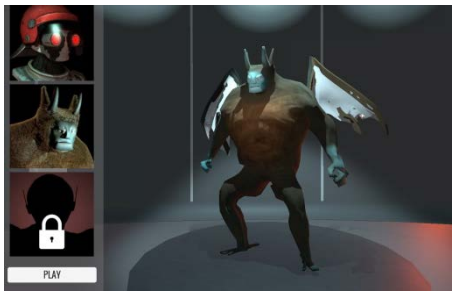


Additionally, it was determined that the current Soliton system is not ready for use. During the Vicon testing session only 2 of the anticipated 6 Solitons were working. The lengthy calibration process of the Solitons resulted in only 10 useable 60 second collections. Dr Khan and Ms. Zhao have been working on a more dependable system and will deliver Soliton version 3 (v3) on Oct 5.

In the interim, Dr. Lowes and her team continue to improve the current Kinect ACTIVE system as it was determined to be the

more accurate measure of functional reaching volume at this time. Improvements to the Kinect ACTIVE system include the development of a standardized tutorial that provides standardized instructions to every subject that plays the game and therefore minimizes any bias that may occur if a different clinical evaluator has the subject play than a previous trial. Voice-overs to read the tutorial at the beginning of the trial and provide standardized encouragement throughout the trial are currently under development.

vi. Develop ACTIVE-Soliton functional reaching volume game



Jeremy Patterson and his team developed an interactive functional reaching volume game that is compatible for both the ACTIVE-Soliton system and the Kinect-based ACTIVE system. The subject is able to select a character from two options (Figure XX). The subject then uses his arms to guide the character through a fantasy course. Maximal leaning and reaching is encouraged by having the character collect coins and avoid robot-like characters that appear throughout the course (Figure XX).

The subject leans and reaches to "fly" the character through the 65-second course before the character reaches a mission intermission platform. This serves as a rest break for the subject and the character resumes the mission when the clinical evaluator selects the "continue" option. The subject then guides the character through another 65-second course and then lands at the final platform. Upon completion of the mission, a screen appears that states the mission was accomplished and shows the score (calculated by the number of coins collected) to the subject. The two aspects of the mission serve as two separate trials, similar to the 2 trials completed in the Kinect ACTIVE. The functional reaching volume is recorded along with the trunk excursion in both lateral and forward directions.

3) <u>Perform clinical testing and refinement with ACTIVE-Soliton</u>

i. Testing on 15 subjects with DMD and 15 healthy controls

Dr. Khan and Ms. Zhao delivered 6 Solitons to Dr. Lowes on 03 November 2016. Two control subjects and five subjects with DMD played ACTIVE using both the Kinect and Soliton motion tracking sensors. The Solitons were attached to the subject's sternum and upper extremities. The subject played the current Kinect-based ACTIVE game while the solitons simultaneously recorded data in order to compare the two systems for initial validity. In this trial, some technical issues with the Solitons were discovered including difficulty with calibration and battery life that made clinical integration difficult. Dr. Khan and Ms. Zhao used this information to develop Solitons v2.

Following the testing difficulties in the Vicon lab (See section 2i paragraph 2) This goal was tentatively put on hold until a more dependable system (Soliton v3) is delivered.

Specific Aim 2: Establish the natural rate of change in FRV in boys with DMD and quantify the Minimal Clinically Important Difference (MCID) in FRV in boys with DMD.

1) <u>Collect longitudinal data with ACTIVE-Soliton</u>

Due to the unforeseen technical issues with the Solitons, no longitudinal ACTIVE-Soliton data has been collected. However, 33 subjects with DMD have completed baseline and 6-month follow-up visits with the Kinect ACTIVE system. The analysis to determine the natural rate of change in FRV in DMD will be completed in Year 2.

2) Collect functional data and patient-reported outcomes in boys with DMD.
In order to determine the minimal clinically important difference (MCID) in ACTIVE, the change in FRV over time will be compared to results on other functional assessments and patient-reported outcomes that are administered as a standard of care in our clinic. In Year 1, 107 boys with DMD played ACTIVE. The physical therapist determined which functional assessments were appropriate for each patient including questionnaires from Patient-Reported Outcomes Measurement Information System (PROMIS) that are focused on upper extremity function (Pediatric- n=40, Parent-proxy- n=30) and mobility (Pediatric n=8, Parent-proxy n=9), 100 Meter Timed Test (n=45), Six Minute Walk Test (n=43), 10 meter walk/run (n=67), North Star Ambulatory Assessment (n=61), Time to Rise (n=58), and 4 Stair Climb (n=41). Statistical analysis to determine the MCID for ACTIVE will be completed in Year 2.

What opportunities for training and professional development has the project provided? .

John Luna, a graduate student at The Ohio State University's Advance Computing Center for the Arts and Design, interned in virtual environment design/ development at Nationwide Children's Hospital under the guidance of Jeremy Patterson, lead of User Experience Technology Research and Development, to develop the ACTIVE-Soliton functional reaching volume game. John was able to gain professional experience and was a vital contributor to the development of the ACTIVE-Soliton functional reaching game. He conceptualized the graphics for the game and developed the game under the direction of Jeremy Patterson. Due to his contribution to this project and others, he was offered a full-time position after graduation as a Full-Stack Application Developer in the Research and Development department at Nationwide Children's Hospital.

How were the results disseminated to communities of interest?

ACTIVE was presented at several scientific and family meetings during the Year 1 grant period. Specific conference details are below.

- 2017 Parent Project Muscular Dystrophy Annual Connect Conference Chicago, IL
  Tina Duong, MPT presented "Outcomes- Current and Forthcoming Outcome Measures" in the Our New Duchenne Basics- Care, Data, Trials, and Outcomes session. She described ACTIVE and its potential for use in clinical trials in DMD regardless of ambulatory status.

- 21st Annual Cure SMA International Researcher Meeting
  Orlando, FL
  Linda Lowes, PhD presented "Utility of ACTIVE Workspace Volume as a Clinically Meaningful Measure of Upper Extremity Function." She outlined the ACTIVE development process, its use in DMD, and also discussed its potential for use in the spinal muscular atrophy (SMA) population.

- 2017 Myotubular Myopathy- Centronuclear Myopathy Family Conference
  Nashville, TN
  Lindsay Alfano, DPT presented "Motion assessments in individuals with XLMTM." She discussed ACTIVE's potential use in this population and the ongoing research in DMD.

In addition to the scientific and family meetings listed above, ACTIVE was also presented at the Sixth Annual Nationwide Children's Hospital/ OSU/ Wellstone Myology Course in Columbus, Ohio. This course is oriented toward MD and PhD trainees to provide specialized training of neuromuscular disease. Linda Lowes,

PhD lectured the trainees about the importance of outcome measure development and selection and discussed ACTIVE's ongoing refinement, development, and utility as an outcome assessment in clinical trials.

Dr. Lowes and her team visited a local elementary school to teach the students about careers in science/ research and ACTIVE. The students were able to play ACTIVE during their physical education class and ask the team any questions they had.

What do you plan to do during the next reporting period to accomplish the goals?

We will continue to enroll new subjects with DMD into the ACTIVE study as well as increase the number of longitudinal data points we have for existing subjects. The current ACTIVE system was found to be more valid and reliable than the Solitons' current level of development when compared to the gold standard Vicon motion capture system. Therefore, we will move forward with the current ACTIVE system and determine the MCID and natural rate of change in patient with DMD. We plan to use these results to submit a finalized Drug Development Tool Qualification Program for ACTIVE.

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

Research in the field of neuromuscular disease, particularly in Duchenne muscular dystrophy is increasing at an astonishing pace. In order to determine if a potential treatment is efficacious, change has to be detected by the designated outcome assessment. Most of the current clinical trials in DMD use the Six Minute Walk Test (6MWT) as the outcome assessment, which excludes individuals in the late-ambulatory or non-ambulatory phase. In addition if a subject loses ambulation during the clinical trial period, that data is lost as he can no longer complete the primary outcome measure. An outcome measure that is able to detect change on a continuous scale across the spectrum of disease would increase the recruitment pool for clinical trials as well as allow researchers to better understand the potential treatments' impact on later stages of DMD.

ACTIVE has the potential to serve as this outcome measure using the Kinect camera to quantify functional reaching volume while the subject plays an interactive video game. A preliminary data show ACTIVE is a valid and reliable assessment of function (Lowes, 2015). Three areas of improvement were identified in order to implement ACTIVE across the spectrum of abilities in DMD. The first is to ensure all individuals can be recorded. The second is to eliminate the floor effect by improving quantification of small movements. The third is to improve measurement accuracy. The expertise of Dr. Furrukh Khan and Jessie Zhao was leveraged to address the above areas of improvement. Dr. Khan and Ms. Zhao developed miniature wireless motion capture sensors, called Solitons that are able to be implemented into the current ACTIVE system to determine if they improve the current system.

In comparison to the gold standard Vicon motion capture system, the current Kinect-based ACTIVE was more valid and reliable than the current Soliton software. Dr. Khan and Ms. Zhao are currently using these findings to improve the Solitons. In the meantime, Dr. Lowes and her team are continuing to collect data with the current ACTIVE system and address the current obstacles. To this end, a standardized tutorial has been added to the video game as well as standardized encouragement throughout the trial in order to minimize evaluator bias. Currently, the tutorial and encouragement appear as text on the screen. The next step in development is to add voice-overs to read this text.

As more longitudinal ACTIVE data is collected, analysis will be conducted to determine the natural rate of change in functional reaching volume in DMD as well as the minimal clinically important difference (MCID).

This information will allow researchers to determine if a potential treatment is slowing the rate of progression and if the difference is meaningful to the subjects.

What was the impact on other disciplines?

ACTIVE, originally developed for use in Duchenne muscular dystrophy, has the potential to be utilized in other patient populations as well. Dr. Lowes is currently collecting data to determine the utility of ACTIVE in other neuromuscular disorders including spinal muscular atrophy (SMA), limb girdle muscular dystrophy (LGMD), myotubular myopathy (MTM), and DMD carriers. Preliminary data has supported ACTIVE's reliability and validity in the above listed populations. Submission of the SMA ACTIVE data for publication is planned for 2018.

ACTIVE may also be useful in other patient populations outside of neuromuscular disorders. For example, ACTIVE may be able to be used in rehabilitation settings post-cerebral vascular accident and/or spinal cord injury to quantify reaching abilities and compare to the non-affected side. These areas will be explored after development of ACTIVE in DMD is complete.

What was the impact on technology transfer?

Upon completion of the project goals including quantifying the natural rate of change and determining the minimal clinically important difference (MCID) of functional reaching volume in DMD, ACTIVE will be available to other institutions for use in clinical and research settings. The Muscular Dystrophy Association (MDA) Clinic at Nationwide Children's Hospital currently uses ACTIVE as a standard of care functional assessment. There are ongoing initiatives to standardize care in DMD, including physical therapy functional testing, across MDA Clinics. ACTIVE may be a useful addition to the standardized battery of assessments that would fill a void of a functional assessment that spans the entire disease process and is able to quantify change on a continuous scale.

What was the impact on society beyond science and technology?

Implementation of ACTIVE as a clinical outcome assessment in clinical trials will improve access to experimental treatments to individuals with DMD who have previously often been excluded due to the inability to complete the Six Minute Walk Test (6MWT). Allowing access to clinical trials to those who are no longer ambulatory may increase hope and improve interest in research, which will in turn continue to advance the field of DMD research.

The non-ambulatory cohort of individuals with DMD is a historically underserved population in terms of research. Increased understanding of disease processes in the late stage of disease may lead to improved policies and decision making practices in terms of clinical care for these individuals.

5. CHANGES/PROBLEMS: The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

Implementation of Solitons into the current ACTIVE system

Delay: The implementation of Solitions into the current ACTIVE system was delayed due to unforeseen issues with the Soliton software. Dr. Khan and Ms. Zhao identified areas for improvement in the Solitons that need to be address prior to integrating the Solitons into the data collection phase.

Actions for resolution: In the meantime, Dr. Lowes continues to move forward with the other objectives of this project. Enrollment in the current ACTIVE system is ahead of schedule. In addition, refinement of the ACTIVE game by adding the tutorial and standardized encouragement has taken place despite the delay in Soliton integration. Dr. Khan and Ms. Zhao report that the Soliton software is nearing completion after making improvements to the sensors that were identified in the comparison to the gold standard Vicon motion capture system.

The Solitons will be analyzed compared to the current ACTIVE and Vicon systems as soon as the revisions are complete. This is planned for Quarter 1 in Year 2. Should the ACTIVE system be a better assessment of functional reaching volume (FRV) than the Solitons, the focus will be shifted to quantify the natural rate of change in FRV and minimal clinically important difference (MCID) using the Kinect-based ACTIVE system.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects
Nothing to Report

Significant changes in use or care of vertebrate animals.
Nothing to Report/ Not Applicable

Significant changes in use of biohazards and/or select agents
Nothing to Report/ Not Applicable

6. PRODUCTS:

- **Publications, conference papers, and presentations**
  Nothing to report

- **Journal publications.**
  Nothing to Report

Books or other non-periodical, one-time publications.
Nothing to Report

Other publications, conference papers, and presentations.

Lowes LP. (June 2017). Utility of ACTIVE Workspace Volume as a Clinically Meaningful Measure of Upper Extremity Function. Lecture at the 21st Annual Cure SMA International Researcher Meeting. Orlando, FL.

Alfano LN. (July 2017). Motion assessments in individuals with XLMTM. Lecture at the 2017 MTM-CNM Family Conference. Nashville, TN.

Lowes LP, Alfano LN. (August 2017). Clinical outcome measures in neuromuscular disease. Lecture at the Sixth Annual Nationwide Children's Hospital/OSU/Wellstone Myology Course. Columbus, OH.

- **Website(s) or other Internet site(s)**

  Nothing to Report

- **Technologies or techniques**

  Nothing to Report

- **Inventions, patent applications, and/or licenses**

  Nothing to Report

- **Other Products**
  Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Linda P. Lowes
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Dr. Lowes has performed work in the area of study design, data collection, data analysis, and collaboration with other disciplines.

Funding Support:

Name: Lindsay A. Alfano
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Dr. Alfano has performed work in the area of study design, data collection, data analysis, and collaboration with other disciplines.

Funding Support:

Name: Margaret Dugan
Project Role: Research Aide
Researcher Identifier (e.g. ORCID ID):

Nearest person month worked: 6

Contribution to Project: Ms. Dugan has performed work in the area of data collection, data cleaning, and administrative tasks.

Funding Support:

Name: Furrukh Khan
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Dr. Khan has performed work in the area of data collection and development of the Soliton system.

Funding Support:

Name: Jessie Zhao
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Ms. Zhao has performed work in the area of data collection and development of the Soliton system.

Funding Support:

Name: Jeremy Patterson
Project Role: Consultant
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Mr. Patterson has performed work in the area of ACTIVE-Soliton game development and Soliton calibration process improvement.

Funding Support:

Name: John Luna
Project Role: Graduate Student/ Intern
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2

Contribution to Project: Mr. Luna has performed work in the area of ACTIVE-Soliton game development and Soliton calibration process improvement.

Funding Support:

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period? Nothing to report

What other organizations were involved as partners?

IKOVE Venture Partners:
Columbus, OH
Partner's contribution to the project

- In-kind support

- Collaboration

The Ohio State University Advanced Computing Center for the Arts and Design Motion Lab: Columbus, OH
Partner's contribution to the project

- Facilities

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to **https://ers.amedd.army.mil** for each unique award.

Not Applicable

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

Not Applicable

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.